12. (Amended) A cocount foliar decay virus DNA fragment comprising the stem-loop structure set forth in SEQ ID NO:2, but not the translation start for the open reading frame ORF1 set forth as nucleotides 1004 to 1006 of SEQ ID NO:1, wherein the DNA fragment has promoter activity.

13. (Amended) A cocount foliar decay virus DNA fragment according to claim 1, which additionally does not contain the translation start for the open reading frame ORF2 set forth as nucleotides 1215 to 1217 of SEQ ID NO:1.

14. (Amended) A cocount foliar decay virus DNA fragment according to claim 1, wherein the DNA fragment further comprises nucleotides 655 to 676 and 682 to 701 of SEQ ID NO:1.

15. (Amended) A cocount foliar decay virus DNA fragment according to claim 1, comprising the nucleotides 211 to 991 of SEQ ID NO:1, 409 to 991 of SEQ ID NO:1, 611 to 991 of SEQ ID NO:1 or 711 to 991 of SEQ ID NO:1.

16. (Amended) A DNA fragment, which is a conserved variant of the sequence set forth in SEQ ID NO:1 or fragment thereof wherein the fragment is a modified promoter which does not have an activity 20% more than or 20% less than the promoter activity of nucleotides 211-991 of SEQ ID NO:1.

17. (Amended) A method of expressing a nucleic acid comprising transfecting a cell one or more DNA fragments according to Claim 12.

18. (Amended) The method of claim 17, wherein the cell is a bacteria, yeast or fungi cell.

19. (Amended) A method of expressing a gene in a plant comprising transfecting one or more DNA fragments according to Claim 12, wherein the expression is tissue specific.

20. (Amended) The method of claim 19, wherein the tissue specific expression occurs in phloem cells.

21. (Amended) A method of producing chimeric constructs comprising, transfecting one or more DNA fragments according to Claim 12.

22. A transgenic plant, part of a plant, transformed plant, yeast or bacterial cells comprising a DNA according to Claim 12.

23. (New) A cocount foliar decay virus virus DNA fragment comprising the stem-loop structure set forth in SEQ ID NO:2, but not the translation start for the open reading frame ORF2 set forth as nucleotides 1215 to 1217 of SEQ ID NO:1, wherein the DNA fragment has promoter ~~aetivity.~~

24. (New) A cocount foliar decay virus DNA fragment according to claim 1, wherein the DNA fragment further comprises nucleotides 734 to 785 of SEQ ID NO:1.

25. (New) The DNA fragment of claim 24, wherein the DNA fragment further comprises nucleotides 655 to 676 and 682 to 701 of SEQ ID NO:1.

II. REMARKS

Claims 12-25 are pending in the application after entry of his amendment. Claims 11-22 have been rejected. Applicants appreciate the careful reading by the Examiner regarding the correct numbering of the claims.

Applicants note that a Certified copy of the German Priority document has not been filed with the PTO, but a translation of same has been provided. Please indicate whether Applicants need to submit a Certified copy of the German Priority document.

A new Sequence Listing under 37 C.F.R. §§ 1.821-1.825 is submitted herein. The content of the paper copy and the computer readable form of the Sequence Listing are the same. No new matter is believed to be added by the Sequence Listing, as support for the sequences comes from the specification or the literature.

SEQ ID NO:1 has been changed. SEQ ID NO:1 is still 1291 nucleotides long and contains the same nucleotides as the original SEQ ID NO:1, however, the starting nucleotide has been changed, because it was realized that the application is written from a different reading frame, than the sequence as originally presented. It was realized that the numbering scheme throughout the specification refers a linear sequence of the circular CFDV DNA created by an XhoI restriction digest (see page 3, line 38 -page 4,line 5 of the specification which sets forth the numbering scheme for the application). It appears that the sequence presented in Rhode et al., the inventors' publication, while containing the XhoI site, was re-orientated for publication so that the start sites of the ORF1, ORF2, ORF3, were near the beginning of the sequence. Table 1 lists the positions of the various important structures contained in the CFDV DNA as set forth in the specification. In addition, figures 2-4 provide specific sequences of the stem loop region as well as the TATAA and Rpt1 and Rpt2 regions respectively. Based on this it is clear that Rpt1 must start at 655 of the sequence. Finding the sequence of Rpt1 in the original SEQ ID NO:1, reveals that Rpt1 does not start at 655, but rather starts at nucleotide 1054. Using Rpt1 as an anchor, SEQ ID NO:1 has been modified so that nucleotides 1-390 of original SEQ ID NO:1 have been moved to the end of the sequence such that they are now nucleotides 902-1291. Thus, position 1 of the new SEQ ID NO:1 was position 391 of the previous SEQ ID NO:1. A review of this sequence with subsequent matching of the corresponding sequences as denoted in Table 1 and set forth in Figures 2-4, shows that the nucleotides are in the same order except for the change noted above. In addition, the ORF1, which Table 1 indicates starts at 1004, shows an ATG start position at 1004 of the new sequence as well as the indicated AUG start for ORF2 at position 1215.

Claims 12-15 have been amended to refer to "cocount foliar decay virus" rather than just CFDV virus as suggested by the Examiner. This amendment does not narrow the claims as the claims were clear as written, given that one of skill in the art would understand CFDV to refer to cocount foliar decay virus. Furthermore, this amendment was not made for reasons related to patentability because the claim was clear as originally written.

Claims 12-15 have been amended to refer to SEQ ID NOs where appropriate as suggested by the Examiner. This amendment does not narrow the scope of the claims, nor was it made for reasons related to patentability.

Claims 12-16 and 22 were amended to include an appropriate article and to correct any other issues related to the addition of the article. This amendment does not narrow the scope of the claims, nor was it made for reasons related to patentability as the claim was clear and unambiguous as originally written.

Claims 17-22 have been amended to correct their dependencies. This amendment does not narrow the scope of the claims, nor was it made for reasons related to patentability as the claim was clear and unambiguous as originally written.

Claim 16 has been amended to refer to "A DNA fragment, which is a conserved variant of the sequence set forth in SEQ ID NO:1 or fragment thereof wherein the fragment is a modified promoter which does not have an activity 20% more than or 20% less than the promoter activity of nucleotides 211-991 of SEQ ID NO:1." Support for this amendment can be found at least page 5:lines 14-24 where mutations are described. Claim 16 has also been amended to remove the phrases, "the starting fragment," "derived from, " "modifying individual nucleotides or smaller groups of nucleotides," and "comparable." This Amendment does not narrow the claim as amended claim 16 is not narrower in scope then original claim 16. Furthermore, this amendment was not made for a reason related to patentability as the claim was clear and unambiguous as previously written.

Claims 17-21 have been amended to provided a step to the method. Support for these amendment can be found at least in the examples, where transfection of the disclosed nucleic acids is described.

Claims 14 has been amended to recite additional structural elements, the Rpt structures described in the specification. Support for this amendment can be found at least in Table 1.

Claim 22 has been amended to read "comprising a DNA." This Amendment does not narrow the claim. Furthermore, this amendment was not made for a reason related to patentability as the claim was clear and unambiguous as previously written.

New claims 23-26 have been added. New claim 23, is similar to claim 12, but rather is drawn to the lack of ORF2, rather than ORF1. New claim 24 is drawn to claim 1, further comprising the 52 base region defined by nucleotides 734-785 of SEQ ID NO:1. Support for this claim can be found at least in Table 1. New claim 25 is drawn to both the Rpt regions and the 52 base region. Support for this amendment can be found at least in Table 1.

III. ARGUMENT

A. Objections

The objections to claims 12-15 for allegedly referring to an acronym in the claims prior to defining the acronym, to claims 12-15 for referring to nucleotide sequences without having corresponding SEQ ID NOs, to claims 12-16, and 22 for lacking articles, and to claims 11, and 17-22 for having incorrect dependencies are believed to now be moot in light of the non-narrowing claim amendments made herein. Withdrawal of these objections in light of the amended claims is respectfully requested.

B. Rejection under 35 U.S.C. § 112, second paragraph

Claims 11, 16, 17-21, and 22 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite and failing to particularly point out the claimed subject matter.

The PTO has rejected claims 11 and 22 under 35 U.S.C. § 112, second paragraph for the phrase "obtained using a DNA according to claim," claim 16 for the phrases "the starting fragment," "derived from, " "modifying individual nucleotides or smaller groups of nucleotides," and "comparable," and claims 17-21 for not reciting a step in the claimed methods. Claims 12-22 have been amended to recite a step in the methods, and therefore this rejection is respectfully traversed, and allowance of claims 12-22 is earnestly requested.

C. Rejection under 35 U.S.C. § 101

Claims 17-21 were rejected under 35 U.S.C. § 101, for allegedly improperly defining a process. The examiner specifically pointed out that no steps were set forth in the method of using claims. This rejection is respectfully traversed as applied to the amended claims, which now recite a step.

D. Rejection under 35 U.S.C. § 112

1. Introduction

The disclosed subject matter revolves around promoters that can function in both monocot and dicot plants, as well as in the phloem tissue of plants. As discussed in the specification, this function requires two structural elements, 1) the stem loop region of the CFDV DNA and 2) the absence of at least one of the translation start sites for either ORF1 and/or ORF2. The Applicants have provided examples of many variants of the disclosed promoter regions that have the required elements. The Examples, support the assertion that the only required elements are these two elements.

2. Enablement

Claims 11-22 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled.

a) Claims are fully enabled

The Examiner appears to question two issues: 1) the claims allegedly cover promoter regions that do not have promoter activity, and 2) and the claims allegedly cover any modification of the promoter region.

With respect to the promoter activity, the claims have been amended to specifically recite the requisite promoter activity. This addresses the Examiner's concern regarding the promoter activity. It is understood that the Applicants are not giving up nucleic acid molecules related to other components of the promoter region of the CFDV DNA as these regions can be used in a

promoter containing the required elements or they can also be used for example as probes or primers.

With respect to the claims covering any modification of the promoter region, the claims are fully enabled for modifications to the promoter region, as long as the modified promoter regions have the stem-loop structure associated with the promoter region and lack the ORF1 and/or ORF2 start sites in the promoter region. All of the claims require that these elements be present. The Examiner in fact agrees with this stating, "The specification teaches deletions in the CFDV . . . promoter region which comprises the stem loop structure and which still maintains promoter activity." Thus, the PTO admits that the specification teaches that which is claimed. The deletions in the ORF1 and/or ORF2 start sites add to the desired activity, but the presence of the CFDV DNA stem loop region is required.

Contrary to the position of the PTO, the deletion experiments set forth in the specification, are compared to CaMV 35s promoter region, not the CF4 fragment. (See page 12, lines 27-34.) Also the PTO is correct that Table 1 sets forth a number of deletion variants of the claimed promoter regions; however, these variants are not only of the ORF regions, these variants are of large sections of the promoter region itself.

The PTO states, "In view of the claims that encompass the promoter as stated above, encompassing and substitution, deletion insertion or modification of nucleotides and still maintains promoter activity the specification *does not provide any guidance*. The specification *does not provide any guidance* as to what these modifications are and why one would try to ma[d]ke these modifications." (emphasis added, page 6 of Office Action). Applicants respectfully direct the PTO to Table 1 and Table 2 of the specification where sufficient examples of the exact type of information the PTO seeks *is* provided. Furthermore, the PTO has indicated this very fact at another location in the Office Action stating "Applicants results demonstrate numerous constructs comprising various regions of the entire stem loop structure and deletions in the ORF1, 2, and 3 regions." These "numerous constructs . . . [and] various regions" indicate that massive alterations can be made in the promoter region while maintaining function if the

stem-loop structure is present. This is the very type of data needed to support the full breadth of the claim subject matter. One of the skill in the art clearly understands that a point mutation or other alteration can take place, for example, in the region between 211 and 411 of SEQ ID NO:1 since the entire region can be deleted and function is still maintained. This is not an example of an inventor not having made variants of the claimed subject matter, or just making minor variations of the claimed subject matter which do not represent the full scope of the claim. What more would the PTO have the Applicants do? Make all possible variants. Surely, the standard of undue experimentation as outlined by *Wands* would not require such an unreasonable amount of work on the inventor himself. Especially in situations, such as this, where the Applicants have provided variants across the full scope of the claim, ie. deletion mutants lacking nucleotides 211 to 411 of SEQ ID work, deletion mutants lacking nucleotides 211-611 of SEQ ID NO:1 work, and even deletion mutants lacking nucleotides 211-711 of SEQ ID NO:1 work. Furthermore, the variants provided in the specification lack massive regions of the ORFs of the CFDV DNA and they still function. In fact, the CFDV DNA is 1291 nucleotides long, and the Applicants data indicate that promoters as small as 280 nucleotides (see CF5) still function.

Contrary to the position of the PTO, making mutations in the promoter region would not be trial and error, given the level of guidance provided by the Applicants. Those of skill in the art based on the present disclosure, surely would be able to predictably make functional mutants at will in any region of the disclosed promoter region, provided the skilled artisan retained the stem-loop structure in the constructs as recited in the claims.

b) *PTO's legal standard incorrect*

Notwithstanding the above, and the fact that very little experimentation would be required to practice the invention, the PTO's position that routine screening is grounds for non-enablement is, respectfully, incorrect. The standard of undue experimentation does not prevent screening of many non-working examples to find a few examples that function as claimed.

(1) Standard

One determines undue experimentation not by analyzing a single factor, but rather by analyzing and weighing many factors. The legal standard set out in *In re Forman* 230 U.S.P.Q. 564, 547 (Bd. Pat. App. & Int. 1986) and elucidated in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400 (Fed. Cir. 1988) sets forth the following factors for consideration: (1) The quantity of experimentation necessary (time and expense); (2) The amount of direction or guidance presented; (3) The presence or absence of working examples of the invention; (4) The nature of the invention; (5) The state of the prior art; (6) The relative skill of those in the art; (7) The predictability or unpredictability of the art; and (8) The breadth of the claims. It is not necessary that every enablement analysis consider all of the factors. *Amgen, inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991).

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *M.I.T. v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 190 U.S.P.Q. 214 (CCPA 1976).

The facts underlying the decision of *In* re *Wands* illustrate well the concepts put forth in *M.I.T. A.B. Fortia* and *In re Angstadt.* The method claims at issue in *Wands* involved the use of an antibody wherein the "antibody is a monoclonal high affinity IgM antibody having a binding affinity constant for . . . [the antigen] of at least 10^9M^{-1}." *In re Wands*, 858 F.2d at 734. This claim covers *any* monoclonal antibody, not just a specific monoclonal antibody, and the PTO argued that the Applicant failed to enable *all* monoclonal antibodies. *Id.* Briefly, the skilled artisan generates monoclonal antibodies by injecting an antigen into a host animal causing an immune reaction, isolating spleen cells, some of which produce the antibodies that bind the antigen, fusing the spleen cells with a cancerous myeloma cell producing a hybridoma, and then screening individual hybridomas to isolate those that produce antibodies that bind the antigen. *Id.* at 733-734. The PTO supported its non-enablement position by pointing out that 1) not all

hybridomas produce antibodies that bind antigen, 2) not all hybridomas that bind antigen will bind with an affinity of $10^9 M^{-1}$, and 3) the Applicants own data indicated that a small percentage of hybridomas actually produced monoclonal antibodies which fell within the scope of the claims. *Id.* at 738-739. The court rejected these arguments by stating,

> cell fusion [hybridoma technology] is a technique that is well known to those of skill in the monoclonal antibody art, . . .[t]here was a high level of skill in the art at the time when the application was filed, and all the methods needed to practice the invention were well known . . . [and] it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened, . . .[and since] Wands carried out his entire procedure three times , and was successful each time in making at least one antibody that satisfied all of the claim limitations . . . Wands evidence thus effectively rebuts the examiner's challenge to the enablement of their disclosure.

Id. at 740. Furthermore, the Wands court made clear that the amount of and type of experimentation considered undue fluctuates for each type of art. *Id.* The quantity of experimentation lacks relevance outside an assessment of what is "routine experimentation" in the art. *Id.* Thus, the huge amount of "experimentation" that the skilled artisan would have to perform to practice Wands' invention: immunizing an animal, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the hybridomas for the desired characteristics, *knowing that many hybridomas would not produce functional antibodies and* ***not*** *knowing which hybridomas would produced claimed antibody*, was not undue experimentation because it was routine experimentation in the art of monoclonal antibody production. *Id.*

The present claims and corresponding enablement rejection closely parallel the situation presented in *Wands* since the art of producing the presently claimed DNA fragments would be considered a routine type of experimentation in the field of recombinant molecular biology even though the PTO incorrectly casts it as complex and burdensome. Furthermore, specific guidance

to the parts of the promoter that can be mutated is provided, and examples of those mutations are provided, thus also reducing the amount of experimentation required to significantly less than was allowed in In re Wands.

The standard set forth by the Examiner, that routine screening for functional mutants is undue, does not represent the standard set forth in Wands, on facts very similar to the facts presented in Wands.

3. Written description

Claims 11-22 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking adequate written description.

The PTO appears to have rejected claims 11-22 under the written description requirement because the specification allegedly only provides a method of isolating the claimed molecules. The PTO states, "Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required." In support of this position, the PTO cites Fiers v. Revel, 25 USPQ2d 1601 (Fed. Cir. 1993), Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), and Fiddes v. Baird, 30 USPQ2d 1481 (Bd of Pat. App. & Int. 1993). In the present application, Applicants have many structurally related nucleic acids.

The facts of the present application are completely different than the facts of each of these cases. In each of these cases, there was no structure at all provided by the patentee/applicant. Only a method for obtaining the other members of the genus was provided. In each of these cases, what the courts focused on was the lack of a structural relationship that existed between the members of the genus. There is a structural relationship in the presently claimed subject matter. The present claims all require the presence of a stem-loop structure related to the stem-loop of a particular CFDV DNA identified by sequence. Thus, all the members of the genus claims presented by the Applicants are structurally related to each other in a predictable way, through the presence of the stem-loop structure. Adequate written description is provided to

indicate to the skilled artisan that the inventors had possession of the claimed subject matter. Furthermore, claims 14, 24, and 25 add still further defined structure to the claims, requiring the disclosed Rpt regions (claim 14), the 52 base region (claim 24) and both of these regions (claim 25) in addition to the stem-loop structure.

Furthermore, applicants have provided a representative number of examples of the genus. This is not an example, of having only one species disclosed and set forth in the specification. For example, Table 1 sets forth numerous examples that have been shown to function as claimed. Therefore, this rejection is respectfully traversed.

E. Double patenting

Claims 11-22 were rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,303,345.

Applicants will submit a Terminal Disclaimer as appropriate when the application is in condition for allowance.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

ATTORNEY DOCKET NO. 23232.0002
SERIAL NO. 09/462,975

No additional fee is believed due. However, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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I hereby certify that this correspondence or anything indicated as attached or enclosed is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202 on the date shown below.

Gwendolyn D. Spratt — 3-27-02

Gwendolyn D. Spratt — Date

Appendix
Marked-up claims

12. (Amended) A cocount foliar decay virus [CFDV virus] DNA fragment [which encompasses] comprising the stem-loop structure set forth in SEQ ID NO:2, but not the translation start for the open reading frame ORF1 set forth as nucleotides 1004 to 1006 of SEQ ID NO:1, wherein the DNA fragment has promoter activity.

13. (Amended) A cocount foliar decay virus [CFDV virus] DNA fragment according to claim 1, which additionally does not [encompass] contain the translation start for the open reading frame ORF2 set forth as nucleotides 1215 to 1217 of SEQ ID NO:1.

14. (Amended) A cocount foliar decay virus [CFDV virus] DNA fragment according to claim 1, wherein the DNA fragment further comprises nucleotides 655 to 676 and 682 to 701 of SEQ ID NO:1 [characterized in that it encompasses the nucleotides 211 to 991 of SEQ ID NO:1, 409 to 991 of SEQ ID NO:1, 611 to 991 of SEQ ID NO:1 or 711 to 911 of SEQ ID NO:1, where, for the purposes of numbering the nucleotides, the 5'-end of the linearized DNA resulting from cleaving the circular CFDV DNA with the restriction endonuclease XhoI, has been assigned the position 1].

15. (Amended) A cocount foliar decay virus [CFDV virus] DNA fragment according to claim 1, [which encompasses] comprising the nucleotides 211 to 991 of SEQ ID NO:1, 409 to 991 of SEQ ID NO:1, 611 to 991 of SEQ ID NO:1 or 711 to 991 of SEQ ID NO:1[, where, for the purposes of numbering the nucleotides, the 5'-end of the linearized DNA resulting from cleaving the circular CFDV DNA with the restriction endonuclease XhoI, has been assigned the position 1].

16. (Amended) A DNA fragment, which is a conserved variant of the sequence set forth in SEQ ID NO:1 or fragment thereof wherein the fragment is a modified promoter which does not have an activity 20% more than or 20% less than the promoter activity of nucleotides 211-991 of SEQ ID NO:1 [which is derived from one of the DNA fragments according to Claim 1 by

substituting, deleting, inserting, or modifying individual nucleotides or smaller groups of nucleotides and has a promoter activity which is comparable with that of the starting fragment].

17. A method of expressing a nucleic acid comprising [Use of] transfecting a cell one or more DNA fragments according to Claim [1] 12 [as promoter].

18. The method of claim 17, wherein the cell is a [Use of one or more DNA fragments according to Claim 1 as promoter] bacteria, yeast[s] or fungi cell.

19. A method of expressing a gene in a plant comprising [Use of] transfecting one or more DNA fragments according to Claim [1] 12, wherein the expression is tissue specific [as promoter for the tissue-specific expression of genes in transgenic plants].

20. The method of claim 19, wherein the tissue specific expression occurs in phloem cells [Use of one or more DNA fragments according to Claim 1 for the phloem-specific expression of genes in transgenic plants].

21. A method of producing chimeric constructs comprising, [Use of] transfecting one or more DNA fragments according to Claim [1] 12 [for the generation of chimeric constructs for the transient and stable expression].

22. A [T]transgenic plant[s], part[s] of a plant[s], transformed plant[s], yeast or bacterial cells [obtained using] comprising a DNA according to Claim [1] 12.

23. (New) A cocount foliar decay virus virus DNA fragment comprising the stem-loop structure set forth in SEQ ID NO:2, but not the translation start for the open reading frame ORF2 set forth as nucleotides 1215 to 1217 of SEQ ID NO:1, wherein the DNA fragment has promoter activity.

24. (New) A cocount foliar decay virus DNA fragment according to claim 1, wherein the DNA fragment further comprises nucleotides 734 to 785 of SEQ ID NO:1.

25. (New) The DNA fragment of claim 25, wherein the DNA fragment further comprises nucleotides 655 to 676 and 682 to 701 of SEQ ID NO:1.